REMARKS

I. Status of the Claims and Support for the Amendment

Claims 1 and 18 are currently amended.

Claims 1, 5, 8, 11, and 18–20 are currently pending.

Support for the amendment to the claims is found in the specification at page 23, lines 6–8.

II. Rejection under 35 U.S.C. § 102

Claims 1, 5, 8, 11, and 18–20 are rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by U.S. Patent No. 6,797,478 B1 (to Zemlan and Campbell), referred to hereinafter as the '478 patent. Specifically, the rejection alleges that:

> US '478 teaches a method of measuring the level of tau in cerebrospinal fluid (CSF) to determine the presence and/or severity of central nervous system (CNS injury) [sic] including but not limited to cerebral inf[arct], cerebral hypoxic injury, cerebral vascular accidents, and/or central nervous system tumors thus meeting the limitations of claims 1 and 18 (Col. 3–5). As claimed "anoxia" and "ischemia" fall into the rubric of "cerebral vascular accident" thus meeting the limitations of claims 1 and 18. US '478 also teaches that tau includes any or all of the six non-cleaved isoforms of tau as well as cleaved forms thus meeting the limitations of claims 1 and 18 (Col. 4–5). US '478 also teaches calibrating the level of tau in CSF based on patients without axonal degeneration versus patients with axonal degeneration (CNS injury) thus meeting the limitations of claims 1 and 18 (Col. 5)
>
> Also the causative agents and/or events of said anoxia and ischemia are also anticipated by US '478 which teaches practicing the method for primary hemorrhages including cerebral hemorrhage and arterial occlusion which includes thrombosis thus meeting the limitations of claims 8 and 19 (Col. 3). US '478 also teaches practicing the method above to "ascertain or predict clinical outcome following such trauma" thus meeting the limitations of claims 11 and 20 (Col. 3).

Applicant respectfully traverses.

As set out in the *MPEP* "'A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art

reference.' *Verdegall Bros. V. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)." *MPEP* § 2131. Applicant asserts that this standard is not met with respect to the claims as currently amended. The currently amended claims require an analysis of the levels of total tau whereas the invention described in the '478 patent is explicitly limited to an analysis of the level of "*truncated*" tau.

Contrary to the claims of the present invention, the '478 patent states, in pertinent part, that:

> [t]he present data indicate that only cleaved tau and not full length 48kDa to 68 kDa tau proteins are present in CSF (Clevland *et al.*, 1977; Couchie and Nunez, 1985). Consistent with these data, differential CSF hybridoma screening identified three Mabs that demonstrated high affinity for the cleaved form of tau found in CSF but limited affinity for intact, full length tau. . . .
>
> The present data indicate that CSF levels of cleaved-tau reflect the extent of CNS axonal degeneration.

'478 patent, Col. 12, lines 1–4, 38, and 39 (emphasis added). Thus, rather than anticipating the instantly claimed invention, the '478 patent actually *teaches away* from the claimed invention. That is, the '478 patent's recitation that "only cleaved tau and not full length 48kDa to 68 kDa tau proteins are present in CSF" would indicate to one of ordinary skill in the art that full-length tau is not present in CSF and could not serve as a useful marker for CNS damage. In contrast, the instant invention demonstrates, and the currently amended claims require, the detection of "total tau" (which includes 48kDa to 68kDa full-length tau) in CSF.

In support of this position, Applicant directs the Examiner's attention to page 23, lines 6-8 of the instant application where it recites: "*CSF-tau levels were determined using a sandwich ELISA (INNOTEST hTAU antigen, Innogenetics, Gent [sic], Belgium), that measured total tau (both normal and hyperphosphorylated tau).*" The Examiner's attention is further directed to Sjögren *et al.* (*J Neurol Neurosurg Psychiatry* 2001; 70:624–630; a copy of which is

enclosed as a part of a Supplemental Information Disclosure Statement), which demonstrates that the INNOTEST hTAU antigen sandwich ELISA provides for recognition of full-length tau in a patient's CSF (*i.e.* 48kDA–65kDA tau). At page 625 the Sjögren *et al.* reference indicates that the INNOTEST hTAU antigen was the sandwich ELISA used (*see* right column, section entitled "CSF ANALYSIS") and in Figure 5 of Sjögren *et al.* shows that the tau recognized using the INNOTEST hTAU antigen sandwich ELISA had molecular weights in the range of 48 kDa to 65kDa (page 627, right column). This unequivocally demonstrates that the "total tau" of the instantly claimed invention includes tau in the size range of 48–65kDa, which tau is *explicitly* excluded by the description of the '478 patent.

Accordingly, Applicant asserts that the instantly claimed invention is novel, under 35 U.S.C. § 102(e), because the '478 patent does not "*set forth*" the measurement of "total tau", rather the '478 patent appears to explicitly limit itself to measurement of cleaved tau. Thus, the "total tau" element is missing in violation of the *Verdegall Bros.* Standard. Moreover, the '478 disclosure explicitly recites that full-length tau (defined as 48kDa to 68kDa tau) is <u>not</u> present in the CSF (*see*, '478 patent, col. 12, lines 2 and 3).

Given the foregoing, Applicant contends that the present invention is novel over the '478 patent. Further, because the '478 patent explicitly *teaches away* from the instantly claimed invention, Applicant believes that the '478 patent cannot, reasonably, be viewed as rendering the current invention obvious.

III. Conclusion

In view of the foregoing AMENDMENT and REMARKS applicant believes that all rejections of and objections to the instant application have been addressed and overcome and that the rejection under 35 U.S.C. § 102(e) may now properly be withdrawn. Consequently,

Applicant respectfully requests favorable reconsideration of the application and issuance of a Notice of Allowance therefor.

The Examiner is invited to contact the undersigned attorney at 713.787.1589 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

Matthew L. Madsen
Reg. No. 45,594
Attorney for Assignee
INNOGENETICS N.V.

HOWREY SIMON ARNOLD & WHITE, LLP
2941 Fairview Park Drive, Box 7
Falls Church, VA 22042
(713) 787-1400

Date: January 27, 2005